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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,362	08/21/2003	Xian-Ming Zeng	NHC19585-USA	8631

7590 10/30/2006

IVAX CORPORATION
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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,362	ZENG, XIAN-MING	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are pending.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on August 21, 2002. It is noted, however, that applicant has not filed a certified copy of the GB 0219512.1 application as required by 35 U.S.C. 119(b).

Specification

Claims 2-10 are objected to because of the following informalities: the word(s) "claim" in said claims is improperly capitalized. Appropriate correction is required.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 5-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Haeberlin (WO 01/39745).

Applicants claim (1) a dry powder composition comprising (a) at least about 0.25% w/w of an active ingredient with a particle size of less than 10 microns in diameter and (b) a pharmaceutically acceptable particulate carrier with a particle size of less than 250 microns in diameter (claim 1) or wherein the active is present in an amount less than 10% w/w (claim 2), wherein the active is formoterol or a pharmaceutically acceptable salt thereof (claims 6-7), the carrier is lactose (claim 5); (2) a capsule containing from 1-25 mg of a dry powder composition

of claim 1 or 4 (claim 8); (3) a MDPI (i.e. a multidose dry powder inhaler) comprising a reservoir containing the dry powder of claim 1 or 4 (claim 9); and (4) a method for the treatment of chronic obstructive pulmonary (COPD) disease by the step of administering the dry powder of claim 1 or 4 (claim 10).

Haeberlin discloses dry powder formulations that are particularly effective for the **treatment of COPD** when administered by inhalation as **a dry powder comprising formoterol in admixture with a diluent or carrier in an amount of 400 micrograms to 5,000 micrograms per microgram of formoterol active** (pg 1, 2nd paragraph). A composition comprising 400 micrograms of diluent and 1 microgram of formoterol active comprises **0.25% w/w active**. Formoterol may be in the form of its free base or in the form of a **pharmaceutically acceptable salt** (pg. 2, lines 1-3). A particularly preferred formoterol salt is **formoterol fumarate**, especially formoterol fumarate dihydrate (pg. 2, 2nd paragraph beginning on said page). **Suitable diluents or carriers include lactose** (pg. 2, last three lines of said page). Lactose is a preferred diluent (pg. 3, line 1). The mean particle diameter of formoterol active (A) is preferably up to 10 microns, especially preferably 1-5 microns (pg. 3, lines 4-6). The **diluent or carrier (B)** has a maximum diameter of 300 microns, **preferably a maximum diameter of 212 microns** (pg. 3, lines 6-8). In a preferred embodiment the dry powder is in a capsule containing a unit dose of (A), wherein the amount of diluent/carrier is preferably such that the **total weight of the dry powder per capsule is between 5 mg to 25 mg** (pg. 3, 2nd paragraph). Doses of formoterol active may be from 1 microgram to 60 micrograms (pg. 3, 2nd paragraph). In another preferred embodiment **the dry powder is in a reservoir of a multi-dose dry powder inhaler (i.e. MDPI)** adapted to deliver a unit dose (pg. 4, 2nd paragraph). Multi-dose dry powder

inhalers are well known in the art and commercially available (pg. 4, 2nd paragraph). Gelatin capsules containing dry powder compositions comprising formoterol fumarate dihydrate in admixture with lactose monohydrate are exemplified in Examples 1-29. Example 6 discloses a composition wherein the formoterol active is present in an amount of 0.24% w/w.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller (WO 00/28979), wherein U.S. Patent No. 6,645,466 is used being used as the English language equivalent.

Applicant's claims 1-2 and 5-7 have been described above in the rejection under 35 U.S.C. §102(b) as being anticipated by Haeberlin. In claims 3-4, Applicant claims dry powder compositions wherein the composition comprises about 0.26 % to about 1% w/w active (claim 3) or about 0.265 % to about 0.5 % w/w active (claim 4), wherein "about" is defined in [0019] of the instant specification to mean a variance of 5% of both the upper and lower limits of stated values in a range of values.

Keller discloses in Example 1 pharmaceutical dry powder formulations with an improved resistance to moisture **comprising 99.23% w/w lactose monohydrate, 0.50 % w/w magnesium stearate, and 0.27 % w/w formoterol fumarate, wherein the lactose monohydrate particles all have a size of less than 200 microns** (see also, title, abstract, and claims). Keller discloses that the pharmaceutically active compounds in the disclosed powder formulations preferably have a mean particle diameter with a maximum of 10 microns, in particular at most a diameter of 5 microns (col. 9, lines 8-16). Keller discloses that the invented dry powder formulations are particularly advantageously **for use in multidose dry powder inhalers, which contain a**

powder reservoir (col. 9, lines 4-7). Keller also discloses that in general the mean particle diameter of the carriers is preferably 50-200 microns (col. 7, lines 50-53), wherein lactose monohydrate is a generally preferred carrier (col. 8, line 7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haeberlin (WO 01/39745).

NOTE: This rejection is being made in favor of compact prosecution and in anticipation of Applicant's amendment of the instant claims to recite an amount of active greater than 0.25% w/w.

Applicant Claims

Applicant's claims 1-2 and 5-10 have been described above in the rejection under 35 U.S.C. §102(b) as being anticipated by Haeberlin. In claims 3-4, Applicant claims dry powder compositions wherein the composition comprises about 0.26 % to about 1% w/w active (claim 3) or about 0.265 % to about 0.5 % w/w active (claim 4), wherein "about" is defined in [0019] of the instant specification to mean a variance of 5% of both the upper and lower limits of stated values in a range of values.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The disclosures of Haeberlin have been set forth above in the instant application.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Haeberlin lacks the teaching of dry powder compositions comprising about 0.26% w/w to about 1% w/w active ingredient.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to optimize the amounts of formoterol in the compositions of Haeberlin according to the needs of subjects in need of administration of formoterol, for example, subjects in need of administration of formoterol to treat COPD. The ratio of formoterol to diluent/carrier disclosed on page 1 of Haeberlin is described as a particularly effective formulation for the treatment of COPD, however, this description of the dry powder compositions as being "particularly effective" does not constitute a teaching away from compositions having greater amounts of formoterol active relative to the diluent/carrier. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states, "whoever invents or discovers any new and useful

process ... may obtain a patent therefor..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 6 be found allowable, claim 7 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 6 and 7 are identical.

Claims 1, 4-7, and 9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 9-11 of copending Application No. 10/646,361 (copending '361) in view of Haeberlin (WO 01/39745). The cited claims of the instant application and copending '361 although different are not patentably distinct, because the claims of both applications are mutually overlapping in scope and obvious. Independent claim 1 of the instant application claims a dry powder composition comprising (a) at least about 0.25% w/w of an active ingredient with a particle size of less than 10 microns in diameter and (b) a pharmaceutically acceptable particulate carrier with a particle size of less than 250 microns in diameter. Independent claim 1 of copending '361 claims a dry powder inhalation composition comprising (a) medicament particles and (b) a mixture of lactose

particles with a VMF of between about 70 and about 120 microns and a diameter of less than 250 microns. Lactose is a known diluent/carrier used in dry powder formulations. Dependent claim 10 of copending '361 claims a dry powder inhalation composition wherein the medicament particles are formoterol fumarate dihydrate. The cited claims of copending '361 lack the express teaching of particle sizes for the medicament particles and the amount of medicament particles in said dry powder compositions. This deficiency is cured by the teachings of Haeberlin, which have been set forth above. It would have been obvious to a skilled artisan to combine the teachings of Haeberlin with those of copending '361 to obtain suggested active to diluent/carrier ratios and suitable active particle sizes useful for dry powders intended for inhalation. A skilled artisan would have had a reasonable expectation of success upon combination of the teaching of copending '361 with those of Haeberlin because both teach dry powder inhalation compositions wherein the active is formoterol and Haeberlin's compositions are particularly effective in the treatment of COPD.

This is a provisional obviousness-type double patenting rejection.

Other Matter

The Examiner respectfully suggests removing the parentheses in claims 1-4 surrounding the words "by weight of the composition" to ensure that said phrase is understood as an intended claim limitation.

Conclusion

Claims 1-10 are rejection. Claims 2-10 are objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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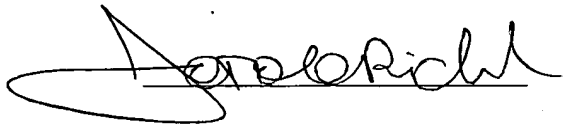

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